DETAILED ACTION

Formal Matters

1. Applicant's Response and Amendments filed 6 September 2007 are acknowledged and entered. Claims 1-8, 10-15, 17-22, and 26-28 are pending. Claims 9, 16, 23-25, and 29 have been cancelled by Applicant. Claims 2-8 are withdrawn, as being drawn to non-elected inventions. Claims 1, 10-15, 17-22, and 26-28 are under examination.

2. In view of recent changes in case law and the recently published Interim Guidelines for Examination under 35 USC 103, (see the Federal Register, Volume 27, No. 195, 10 October 2007, pp. 57526-57535), the art previously cited of record, but withdrawn, is reapplied herein. However, in order to give Applicant an opportunity to respond to the art rejections, set forth below, this action is **NON-FINAL.**

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on 11/7/2007 has been considered. A signed copy is attached hereto.

Response to Arguments/Amendments

Objections/Rejections Withdrawn

4. Rejections drawn to cancelled claims 16, 23, 24, and 29 are moot in light of Applicant's cancellation of the claims.

5. The rejection of claims 1, 10-15, 17-23, 26-28 under 35 U.S.C. 112, first paragraph, scope of enablement is withdrawn.

6. The rejection of claim 10 under 35 U.S.C. 112, second paragraph, is withdrawn in light of Applicant's amendments.

7. The rejection of claims 1, 10, 11, 14, 20, and 21under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn.

Claim Objections/Rejections Maintained

Claim Rejections - 35 USC § 112, First Paragraph

Written Description

8. Claims 1, 12, 13, 15, 17-19, and 22 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, are maintained for reasons of record and for the reasons set forth herein.

Applicant argues that an adequate description of the claimed invention is set forth in the specification such that it shows Applicants were in possession of the claimed genus at the time of filing. In support of their arguments, Applicant cites Enzo Biochem, Inc. v. Gen- Probe, Inc., 63 USPQ2d 1609 (Fed. Cir. 2002), for the proposition that an applicant may show that an invention is complete by a disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that Applicant was in possession of the claimed invention. Applicant also argues the applicability of the Written Description Guidelines because a "description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces See, e.g., 66 Fed. Reg. 1099, 1106 (2001)." Applicant argues that the specification sets forth the structure of the ADNF III core sequence (SEQ ID NO: 2) and the correlating function of treating MS.

Applicant argues that the claimed genus is the group of polypeptides comprising SEQ ID NO:2 and have the disclosed function of treating MS. Applicant sites page 22, line 4 through page 24, line 10 and at page 30, line 1 through page 31, line 11 of the specification in support of their arguments. Applicant argues that the Federal Circuit has made it clear that there is no per se rule regarding inclusion of sequence information in a patent application to support description of a nucleic acid sequence, and by analogy an amino acid sequence "When the prior art includes the nucleotide information, precedent does not set a per se rule that the information must be determined afresh" Capon v. Eshar, 76 USPQ2d 1078, 1084-5 (Fed. Cir. 2005). Applicant also cites Falkner v. Inglis, 79 USPQ2d 1001, 1008 (Fed. Cir. 2006) in support of their argument that even incorporation by reference of known sequences is not required for the written description requirement. Applicant's arguments have been fully considered, but they are not persuasive.

A review of the claim language indicates that the claims are drawn to a method for treating MS comprising administering a composition comprising a genus of ADNF III and ANDF I polypeptides with an active core site of NAVSPSIPQ or SALLRSIPA. It is important to note that the open language of the word "comprising" in claim 1, for example, places no limit on the number or form of amino acid residues that may be on either side of the core sequence of SEQ ID NO: 2 (NAVPSIPQ). Additionally, claims 15

and 22 recite polypeptides of the composition which may encompass up to 44 additional amino acids (about 20 on either side of the recited active core sequence). This translates into a minimum of 4.4×10^{20} possible polypeptide variants, considering only the standard 20 L-amino acids at each position with an unspecified residue. This number increases, when substituting one or more D-amino acids as set forth in claims 12 and 13, 18, and 19. Claims 17-22 are also drawn to a genus of ADNF I polypeptides comprising an active core site comprising SEQ ID NO: 1 (SALLRSIPA), which, in preferred embodiments, may encompass up to 44 additional amino acids. This translates into a minimum of 4.4×10^{20} possible polypeptides, considering only the standard 20 L-amino acids at each position with an unspecified residue. This number would increase if non-standard amino acids or D-amino acids were added, as they are in claims 18 and 19. Even if a polypeptide with an active core sequence of SEQ ID NOs: 1 or 2 would retain the function of the active core sequence, one of skill in the art would still not know anything about the structure of the claimed genus other than the core sequence of 8 or 9 amino acid residues. When viewed in light of the genus of functional polypeptides comprising 44 amino acid residues, the disclosed sequence of 8 or 9 residues, only amounts to 18% and 20% of the protein structure, respectively. A genus of polypeptides where only 18% to 20% of the structure is disclosed (meaning that 80% to 82% of the structure is completely unknown) does not have adequate written description. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the claimed genus. Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features (see, Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 927, 69 USPQ2d 1886, 1895 (Fed. Cir. 2004); accord Ex Parte Kubin, 2007-0819, BPAI 31 May 2007, opinion at p. 16, paragraph 1).

Additionally, the genus of ADNF III polypeptides and the genus of ADNF I polypeptides are highly variable in structure (as shown in the NCBI references recited in the Office Action of 6 July 2006). The structure which is asserted to make up the polypeptide must be clearly and positively specified. The structure must be organized and correlated in such a manner as to present a complete operative embodiment which is adequately described in the specification. The instant disclosure fails to provide an adequate description of a sufficient number of variant ADNF III and ADNF I polypeptides that function to treat MS. The general knowledge and level of those of ordinary skill do not supplement the omitted description because specific, not general, descriptions are needed. While "examples explicitly covering the full scope of the claim language" typically will not be required, a sufficient number of representative species must be included to "demonstrate that the patentee possessed the full scope of the [claimed]

invention." Lizardtech v. Earth Resource Mapping, Inc., 424 F.3d 1336, 1345, 76 USPQ2d 1724, 1732 (Fed. Cir. 2005).

In response to Applicant's arguments directed to species of the genus that are known in the art (under either Capon or Faulkner, *supra*), Applicant is not required to set forth what is known in the art. However, Applicant must show that they were in possession of the genus by reciting sufficient structural and functional characteristics to demonstrate to one of skill in the art that Applicant was in possession of the genus at the time of filing (Vas-Cath Inc. V. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). No *per se* standard is being applied. Rather, the instant claims and speciation are considered in light of Applicant's disclosure and the prior art. In the instant case, one of skill in the art would not recognize from the disclosure that the applicant was in possession of the claimed genus (see, Univ. of Rochester and Ex Parte Kubin, *supra*).

With respect to Applicant's reliance on the Written Description guidelines, "[c]ompliance with the written description requirement is essentially a fact-based inquiry that will 'necessarily vary depending on the nature of the invention claimed" Vas-Cath Inc. v. Mahurkar, 935 F.3d at 1563, 19 USPQ2d at 1117). While the Written Description Guidelines and hypothetical examples in the Synopsis can be helpful in understanding how to apply the relevant law, as it existed in 2001 when the Guidelines were adopted, they do not create a rigid test.

In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus. The specification does not clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed (see *Vas-Cath* at page 1116).

New Claim Rejections

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1, 10, 11, 14, 15, 17, 20-22, and 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Gozes et al., US Patent 6,613,740 (2 September 2003, priority to 7 February 1997) and WO 98/35042 (published 13 August 1998), in view of Brenneman et al., (US PreGrant Publication US 20020111301, published 15 August 2002) (all previously cited of record in the Office Action of 6 July 2006).

The Examiner finds the following facts:

a. The claims are drawn to a method of treating multiple sclerosis (MS) by administering a composition comprising an ADNF polypeptide or its active core site comprising the amino acid sequences NAVPSIPQ or SALLRSIPA.

b. The '740 patent teaches methods of using ADNF III polypeptides for the treatment of neurological deficiencies (abstract), including the amino acid sequence NAVPSIPQ (SEQ ID NO:6), [which is identical to instant SEQ ID NO: 2] and SALLRSIPA (SEQ ID NO: 5), [which is identical to instant SEQ ID NO: 1] (column 3, lines15-19 and 60-67; column 21, lines 15-18; column 44, lines 42-53; column 45, lines 32-). SALLRSIPA (SEQ ID NO: 5) is identified as an ADNF III polypeptide in the '740 Patent (column 20, lines 21-25). The protective effect of ADNF III polypeptides in preventing neuronal cell death is taught at column 3, lines 60-67. Full-length ADNF III is taught at column 3, lines 63-64. The administration of ADNF III

polypeptides to inhibit neuronal cell death associated with a number of other neurological diseases and deficiencies is taught at column 6, lines 33-36. The use of ADNF III polypeptides to treat other neurological disorders is taught at column 6, lines 59-60. ADNF III variant polypeptides, including an ADNF III polypeptide comprising up to about 20 amino acids and at least one of the N-terminus and the C-terminus of the active core site are taught at column 3, lines 38-67 to column 4, lines 1-53; and column 45, lines 43-61; column 49, lines 47-49). Treatment of the neuro-autoimmune disease, Guillian-Barre syndrome, is taught at column 45, line 7. Amino acid sequences with naturally occurring amino acids and amino acid analogs, which include known analogues of natural amino acids that function in a manner similar to the naturally occurring amino acids (i.e. amino acid mimetics and analogs) are taught at column 5, lines 34-64. Administration of the ADNF III polypeptides systemically, intravenously, subcutaneously, intranasally, and orally are taught at column 45, lines 62-67 to column 46, lines 1-20; column 46, lines 31-37; and column 46, lines 60-65). The SALLRSIPA polypeptide, also identified as "ADNF-9" (at column 3, lines 60-61) is taught as being administered concurrently with "NAP" (NAPVSIPQ, SEQ ID NO: 6; taught as "NAP" at column 9, lines 6-7; column 7, line 44; column 59, lines 9-12) (column 60, lines 38-39). Administration of ADNF-14 (a polypeptide which comprises ADNF-9, see column 2, lines 63-64), ADNF-9, and NAP to mice are taught at Figure 16, column 10, lines 1-11; Figure 17, column 10, lines 12-23; and column 60, lines 31-53).

c. The '740 patent does not specifically teach a method of treating multiple sclerosis.

d. WO 98/35042 teaches method of using ADNF III polypeptides for the treatment of neurological deficiencies (abstract), including use of polypeptides with the amino acid sequence NAVPSIPQ (SEQ ID NO:6), which is identical to instant SEQ ID NO: 2 and (SALLRSIPA (as ADNF-I in SEQ ID NO: 5), which is identical to instant SEQ ID NO: 1 (see also, p. 4, lines 15-32 for background on ADNF I and III structure; and SEQ ID NOs; 1, 3, 6, and 10). The protective effect of ADNF III polypeptides in increasing growth and survival of neurons and in the treatment of neurological deficiencies that develop from neurodegenerative disorders is taught at p. 61, lines 27-29. The method for treating neuronal cell death using ADNF III polypeptides is taught at pages 53-64. A list of neurodegenerative disorders and neuro-autoimmune diseases that may be treated with ADNF polypeptides is taught at p. 60, lines 1-32 and page 8, lines 3-19. Page 8 also recites that those of skill in the art will appreciate that the above list [of neurodegenerative disorders] is not exhaustive and that ADNF III polypeptides can be used to treat other neurological disorders (lines 16-18).

e. Brenneman et al., teach the administration of ADNF polypeptides (p. 33, paragraph 0033) to treat conditions related to increased neuronal cell death (p. 1, paragraph 0003).

f. The level of skill of those in the art encompasses skills in the field of molecular biology relating to the treatment of autoimmune diseases.

g. At the time of the invention, there was a recognized problem or need in the art to treat multiple sclerosis.

h. There were a finite number of identified, predictable potential solutions to treat related neurological and autoimmune disorders using an ADNF polypeptide or active core sequence thereof.

i. One of ordinary skill in the art could have pursued the known potential solutions with a reasonable expectation of success because the '740 patent and WO 98/35042 teach the use of ADNF polypeptides and active core sequences thereof for neurological and autoimmune disorders and Brenneman et al., teach the administration of ADNF polypeptides to treat conditions related to increased neuronal cell death.

j. A person of ordinary skill in the art at the time the invention was made would have reasonably know that the ADNF polypeptides and active core sites thereof would have useful in the treatment of neurological disorders, including autoimmune neurological disorders, and would also be useful in the treatment of multiple sclerosis.

A person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a known composition used to treat a specific disorder was obvious to try might show that it was obvious under 35 USC 103. See also, KSR v. Teleflex, 550 US ___, 82 USPQ2d 1385 (30 April 2007).

In view of the facts recited above, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the prior art elements according to known methods to yield predictable results. The prior art teaches all of the limitations of the claimed invention.

Methods of using ADNF III polypeptides including the amino acid sequence NAVPSIPQ and SALLRSIPA to inhibit neuronal cell death and promote neuronal cell growth are taught by both the '740 patent and WO 98/35042. The '740 patent teaches treatment of the neuro-autoimmune disease, Guillian-Barre syndrome, using ADNF polypeptides or their active core sequences at column 45, line 7. WO 98/35042 also teaches a long list of neurodegenerative disorders and neuro-autoimmune diseases that may

be treated with ADNF polypeptides (p. 60, lines 1-32 and page 8, lines 3-19). Page 8 also recites that those of skill in the art will appreciate that the above list [of neurodegenerative disorders] is not exhaustive and that ADNF III polypeptides can be used to treat other neurological disorders (lines 16-18).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to treat MS in a subject by administering a therapeutically effective dose of an ADNF polypeptide or a peptide comprising the active core site thereof (NAVPSIPQ or SALLRSIPA) as taught by '740 patent and WO 98/35042. Treatment would have been predictable because the '740 patent and WO 98/35042 teach the administration ADNF peptides as therapeutics to treat neurodegenerative disorders.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to treat MS in a subject by administering a therapeutically effective amount of an ADNF polypeptide or active core site thereof as taught by the '740 patent, WO 98/35042, and Brenneman et al., with a predictable expectation of success because the '740 patent and WO 98/35042 teach the administration ADNF peptides as therapeutics to treat Guillan-Barre syndrome, and Brenneman et al., teach the use of ADNF polypeptides to treat conditions related to increased neuronal cell death.

One of skill in the art would have recognized that the results of the combination of known polypeptides or their analogs to treat related neurological and autoimmune disorders would have yielded nothing more than predictable results to one of ordinary skill in the art at the time the invention was made.

13. Claims 12, 13, 18, and 19 are rejected in addition to claims 1, 10, 11, 14, 15, 17, 20-22, and 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gozes et al., US Patent 6,613,740 (2 September 2003, priority to 7 February 1997), and WO 98/35042 (published 13 August 1998), in view of Brenneman et al., (US PreGrant Publication US 2002/001301 A1, published 15 August 2002), and further in view of Voet et al., (1995 Biochemistry, 2nd Ed., p. 67) and Goodman et al., (US Patent 4,587,046, 6 May 1986) (all previously cited of record in the Office Action of 6 July 2006).

The Examiner finds the following facts:

a. The claims recite as stated supra.

b. The '740 patent, WO 98/35042, and Brenneman et al., teach as set forth above.

c. The '740 patent does not teach ADNF polypeptides comprising D-amino acids.

d. Voet et al., teach that D-amino acids are more resistant to proteases than their L-amino acid counterparts (p. 67).

e. Goodman et al., teach that incorporation of D-amino acids into peptides is particularly advantageous when those peptides are administered to patients, as the D-amino acids are resistant to proteolysis in vivo (column 9, lines 48-54).

f. The level of skill of those in the art encompasses skills in the field of molecular biology relating to the treatment of autoimmune diseases.

g. At the time of the invention, there was a recognized problem or need in the art to treat multiple sclerosis.

h. There were a finite number of identified, predictable potential solutions to treat related neurological and autoimmune disorders using an ADNF polypeptide or active core sequence thereof.

i. One of ordinary skill in the art could have pursued the known potential solutions with a reasonable expectation of success because the '740 patent and WO 98/35042 teach the use of ADNF polypeptides and active core sequences thereof for neurological and autoimmune disorders and Brenneman et al., teach the administration of ADNF polypeptides to treat conditions related to increased neuronal cell death.

j. A person of ordinary skill in the art at the time the invention was made would have reasonably know that the ADNF polypeptides and active core sites thereof would have useful in the treatment of neurological disorders, including autoimmune neurological disorders, and would also be useful in the treatment of multiple sclerosis.

k. A person of ordinary skill in the art at the time the invention was made would have also reasonably known that L-amino acids could readily be substituted with D-amino acids by well-known means and with routine experimentation. One of skill in the art would have also known that such substitutions are routine and increase the stability of peptides.

A person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a known composition used to treat a specific disorder was obvious to try might show that it was obvious under 35 USC 103. See also, KSR v. Teleflex, 550 US ___, 82 USPQ2d 1385 (30 April 2007).

In view of the facts recited above, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the prior art elements according to known methods to yield predictable results. The prior art teaches all of the limitations of the claimed invention.

Methods of using ADNF III polypeptides including the amino acid sequence NAVPSIPQ and SALLRSIPA to inhibit neuronal cell death are taught by both the '740 patent and WO 98/35042. Treatment would have been predictable because the '740 patent and WO 98/35042 teach the administration ADNF peptides as therapeutics to treat Guillan-Barre syndrome. WO 98/35042 also teaches a long list of neurodegenerative disorders and neuro-autoimmune diseases that may be treated with ADNF polypeptides (p. 60, lines 1-32 and page 8, lines 3-19). Page 8 also recites that those of skill in the art will appreciate that the above list [of neurodegenerative disorders] is not exhaustive and that ADNF III polypeptides can be used to treat other neurological disorders (lines 16-18).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to treat MS in a subject by administering a therapeutically effective dose of an ADNF polypeptide or a peptide comprising the active core site thereof (NAVPSIPQ or SALLRSIPA) as taught by '740 patent and WO 98/35042. Treatment would have been predictable because the '740 patent and WO 98/35042 teach the administration ADNF peptides as therapeutics to treat neurodegenerative disorders.

It would also have been obvious to one of ordinary skill in the art to substitute one or more L-amino acids with one or more D-amino acids because Voet et al., and Goodman et al., teach that the incorporation of one or more D-amino acids into polypeptides would increase the stability of the protein when administered *in vivo*. The person of ordinary skill in the art could have combined the elements as claimed to treat patients with MS. One of skill in the art would have recognized that the results of the combination of known polypeptides or their analogs used to treat neurological and autoimmune disorders, including MS, would have yielded nothing more than predictable results to one of ordinary skill in the art at the time the invention was made.

Conclusion

NO CLAIM IS ALLOWED.

This action is **Non-Final**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cherie M. Woodward whose telephone number is (571) 272-3329. The examiner can normally be reached on Monday - Friday 9:00am-5:30pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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